York Foundation Trust R&D Unit
SOP
R&D/S81

Case Report Form (CRF) Design and Completion

IT IS THE RESPONSIBILITY OF ALL USERS OF THIS SOP TO ENSURE THAT THE CORRECT VERSION IS BEING USED

All staff should regularly check the R&D Unit's website and/or Q-Pulse for information relating to the implementation of new or revised versions. Staff must ensure that they are adequately trained in the new procedure and must make sure that all copies of superseded versions are promptly withdrawn from use unless notified otherwise by the SOP Controller.

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	Date:	17th June 2019
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	Signature:	Signed copy held by R&D Unit
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This SOP will normally be reviewed every 3 years unless changes to the legislation require otherwise

Version History Log

This area should detail the version history for this document. It should detail the key elements of the changes to the versions.

Version	Date Implemented	Details of significant changes
1.0	16th September 2013	
2.0	24th August 2017	Change of author. Minor additions
3.0	15th July 2019	Minor typographical changes. Update to website address.

Contents

1 Introduction, Background and Purpose

The purpose of this SOP is to describe the procedure to be followed when designing, using and completing paper Case Report Forms (CRFs) for a research study that is being sponsored or co-sponsored by the Trust.

A CRF captures all the necessary data for each participant during a research study. The ICH GCP guideline (section 1.11) defines a CRF as: “A printed, optical or electronic document designed to record all of the protocol required information to be reported to the sponsor on each trial subject.” Under usual circumstances for non-commercial, Trust Sponsored studies the CRF will be in paper form.

A CRF is usually used to record data that is copied from original documents (also known as source documents) such as medical records, laboratory reports, x-ray reports etc. However the CRF can sometimes be the first and only document where data items are recorded i.e. the CRF is the source document, for example validated questionnaires and / or in studies involving healthy volunteers. When the CRF is the source document for any item of data, this needs to be clearly identified in the protocol as required by ICH GCP (section 6.4.9).

The design of a CRF and its subsequent completion has a direct impact on the quality of data that are collected and the results of any study are only as good as that data. Consequently CRFs should be designed to enable data to be captured in a precise, clear and unambiguous way thus ensuring standardisation and consistency of data quality

CRFs are regarded as official study documentation by Sponsors and regulatory authorities and, together with source documents, will be closely examined during monitoring, auditing and inspection.

2 Who Should Use This SOP

This SOP is aimed at:

- Chief/Principal Investigators (CI/PIs) of research studies sponsored or co-sponsored by the Trust
- All Trust staff with delegated responsibility for design and/or completion of CRFs
- R&D Unit personnel who manage sponsorship functions on behalf of the Trust
- Study statistician / Data manager
- Study monitor

3 When this SOP Should be Used

The design of a CRF usually starts at the final protocol stage or when major changes affecting data capture are no longer anticipated. The final authorised CRF should be available before the first patient is enrolled into the study and should be approved by the Sponsor.

4 Procedure(s)

4.1 CRF Design

The first step in designing a CRF is to identify all the data that must be collected in order to meet the study's aims and objectives; this will be specified in the protocol. Only information specified in the protocol should be included i.e. a CRF should not capture surplus information.

A well designed CRF needs to include both generic information and study specific information; it will vary in length depending on the complexity of the related study. It may be necessary to include, for example, sections / pages to gather information about demographic characteristics and medical history, specific endpoints, laboratory assessments, dispensing of the investigational medicinal product(s), adverse events and concomitant medications. The CRF may also contain questionnaires and patient diaries. If a study involves more than one visit, the CRF can be simplified by starting the documentation for each visit on a new page and using the visit number as the main title for that section of the CRF.

General points:

- Each CRF page should have a header/footer section containing key information such as the name of the study, CRF version number, protocol reference number, study identifier, site identifier, participant number, form number, visit number and date
- Patient confidentiality should be maintained through the use of a participant ID number rather than name
- Data should be entered in a logical order e.g. the order of study procedures during a particular study visit. This will minimise potential for error especially when data will be transcribed from source documents to the CRF
- Alignment of items, margins, spacing, font, design of text boxes should be consistent throughout the CRF
- Where the data item asks for a response to be chosen from a list, use a standardised answer mode throughout the CRF e.g. use circling or underlining or deleting or ticking a box not a combination of these approaches. Ticking a box tends to be the easiest to complete
- After each section of the CRF, there should be a space for the person who has completed that section of the form to put their name, signature and date of completion
- Include instructions on how to complete the CRF and how to correct erroneous entries. The instructions may be given on a separate page and / or against specific questions / items on the form (see Appendix for example)
- Include a list of all the inclusion and exclusion criteria as per protocol and provide a 'Yes' **and** a 'No' box for **each** criterion which will need to be ticked accordingly by the person undertaking the assessment. Please note that in a Clinical Trial of an Investigational Medicinal Product (CTIMP), eligibility must be confirmed by a medically qualified member of the research team. This can be achieved by providing space for the signature of the medically qualified person to verify his/her agreement to the patient's entry to the study
- Include an entry for confirmation that informed consent has been taken with space for the date and the name of person receiving consent
- Give page numbers for CRF as specific page number / total number of pages e.g. 1 of 4, 2 of 4 etc

Data items:

- Where applicable, ask for data in standard formats providing exact number of boxes and stating units of measurement to ensure comparable values are entered by data collectors

  e.g. Date: □□-□□□-□□□□
  dd-mmm-yyyy

  Height: □·□□ m^2

- Collect raw data where possible rather than calculated data as the latter are much more difficult to check e.g. for age collect date of birth and date of visit rather than just asking for age
- Limit the amount of data collected as 'free text' as this complicates data analysis
- Specify data 'rounding' rules
- Construct questions so that a definite response is required - it will then be clear if an item is 'not applicable' as opposed to 'missing'. Where a response checklist is not exhaustive, an 'other' option should be included with space for comments if appropriate
- Include numeric codes against categorical data responses to assist later data entry and analysis
- If laboratory test results are being recorded into the CRF then insert a box near the data to record whether the value that is entered falls within or outside the normal range for that test. You must be able to refer to standard tables produced by the laboratory for that test. The investigator will need to insert an assessment of the clinical significance of laboratory values outside the reference ranges. Any test that is clinically significant may constitute an AE and needs to be recorded as such.
- Dispensing of the IMP must be recorded (and coincide with visit dates as per protocol). The number of tablets, treatment packs issued or intravenous (IV) infusion bags administered should also be recorded in the CRF. If return of pills/packs is required then a box for the number of returned oral IMP(s) should also be added. Provide a table to insert all concomitant medications/therapies (name, dose, frequency, start/stop dates, ongoing)
- Include a comments section in the CRF e.g. to capture explanations for missing data
- Include an unscheduled procedures page e.g. to record additional measurements that may have been taken in order to monitor an Adverse Event
- Include a page at the back of the CRF to record any changes made to the data initially collected on the CRF.

4.2 CRF Approval for Trust Sponsored Studies

When the Trust is acting as Sponsor for a study, the member of staff acting as Sponsor's representative (or delegate) will determine whether the draft CRF must be approved by the Trust before it can be used to collect data in a study.

While in draft form the CRF should be labelled as such and version controlled as 0.1, 0.2 etc and dated accordingly until it is approved by the Sponsor's representative. After a final version is approved, the CRF should be labelled as version 1.0 and dated accordingly.

If the Sponsor's representative has deemed that approval is necessary, a draft CRF should be submitted to the R&D Unit (research.governance@york.nhs.uk) by the Chief investigator, or member of the research team with delegated authority. The draft CRF will be reviewed by members of the R&D Unit acting on behalf of the Trust as Sponsor. For CTIMP studies, the draft CRF should be submitted as part of the application for 'Sponsorship in Principle'.

The CRF may need to be updated in accordance with protocol amendments. Updated versions must be approved by the Sponsor and version controlled and dated accordingly.

4.3 Entering Data on a CRF

- CRFs should be completed in a timely manner
- Only authorised members of the team (as documented on the study delegation log) should enter data in the CRF
- The CRF should be completed using permanent ink (blue or black). Pencil should not be used
- All entries should be complete and legible
- The header information (i.e. sponsor's protocol number, participant's initials, ID) should be completed consistently throughout the CRF
- All fields should be completed on each page. If data are missing, an explanation for this should be recorded on the comments page
- If a test was Not Performed, '**NP**' should be recorded in the relevant box (es). The reason for not doing the test should be recorded in the appropriate comments section
- Where information is Not Known, '**NK**' should be recorded in relevant box (es)
- Where information is not applicable, write **NA** in the relevant boxes
- All dates should be completed in the format required by the CRF design e.g. 13NOV2008. Partial dates should be recorded as NKNOV2008.

4.4 Correcting Data Entry in a CRF

Any change or correction to a CRF should be dated, initialled and explained (if necessary) and should not obscure the original entry (i.e. an audit trail should be maintained). A record of all corrections with reasons must be kept.

When making changes on a CRF, the use of correction fluid is not permitted.

4.5 Documenting CRF Corrections

All changes/additions or corrections made to CRF **after** initial data were recorded will need to be documented. Design a page at the back of the CRF with a table for recording changes, the date when the change was done and the reason for it.

4.6 Submitting CRFs

The original copy of the CRF needs to be sent to the Sponsor or to the personnel responsible for data management in a timely manner as specified in each protocol/guidelines however see section 4.7 below for requirements to retain copies at Site.

It is good practice for research staff to initial and date the copy when it has been sent to the Sponsor for audit trail.

4.7 Storing CRFs

The research team will need to keep a photocopy of each CRF on site after they have been completed and signed/dated. The CRF should also be stored in a secure and protected environment. This may be in the Site File or a separate folder for each patient, depending on the size of the CRF, but you must ensure that they are separate to any other documents that might reveal the identity of the participant. A file note should be completed should CRFs be kept separately from the ISF for purposes of audit/inspection.

Once completed, no further entries or corrections should be made in the CRF. Any further queries should be documented as part of the data management system e.g. on a data query form.

On completion of the study the CRF (or copies retained at Site) must be archived at Site along with the other required study documents.

5 Related SOPs and Documents

R&D/S09 Set Up and Management of Research Studies

R&D/S29 Data Management

6 Appendix A

Example of CRF Completion Instructions page

7 Appendix B

Example of a Case Report Form

Appendix A:

Example of CRF Completion Instructions page

The CRF needs to include a page for instructions on how to collect data and complete the Form. These should include the following (but not limited to):

- Complete the CRF using a **black ballpoint pen**
- Ensure all entries are complete and legible
- Ensure that the header information (i.e. Sponsor's protocol number, participant's initials and ID) is completed consistently throughout the CRF. If a subject prematurely withdraws from the trial a single line must be drawn across each uncompleted page
- Ensure that all fields are completed on each page or an explanation for missing data is recorded on the comments page
- If a test was 'Not Done' record **ND** in the relevant box(es).
- Where information is 'Not Known' write **NK** in relevant box(es)
- Where information is 'Not Applicable' write **NA** in the relevant boxes
- The Principal Investigator (or a delegate) must sign and date the Study Completion Page to certify accuracy, completeness and legibility of the data reported to the sponsor in the CRF
- Record participant ID and initials (of first, middle, last name) on each page (insert in header before printing the CRF so it appears throughout). The subject initials should be recorded with a dash (i.e. D-L). Ensure initials remain consistent throughout the CRF
- Complete all dates as day, month, year. The month should be recorded in letters rather than numbers i.e. i.e. 13/NOV/2008 rather than 13/11/2008. Partial dates should be recorded as NK/NOV/2008
- Any change or corrections to entries on the CRF must be dated, initialled and explained (if necessary). The original entry should be crossed out with a single line but must not be obscured. The data correction must be written down as near to original entry as possible
- The use of correction fluid is not permitted

APPENDIX B:
Example of a Case Report Form

CASE REPORT FORM 1

Informed Consent Received ☐ **(tick to confirm) Date /Sign** ……

Meets Inclusion Criteria ☐ **(tick to confirm) Date/Sign** ……..

No Exclusion Criteria Apply ☐ **(tick to confirm) Date/Sign** ……

1. D.O.B ☐☐ ☐☐☐ ☐☐
dd *mmm* *yy*

2. Gender (Please tick box)

Male ☐ (1)

Female ☐ (2)

3. Height (cms) ☐☐☐

4. Weight (kgs) ☐☐☐

HIP

5. Side of Affected Hip (Please tick relevant box)

Left ☐ (1)

Right ☐ (2)

6. Date of Primary THA

☐☐ ☐☐☐ ☐☐
dd *mmm* *yy*

7. Date of Revision

☐☐ ☐☐☐ ☐☐
dd *mmm* *yy*

8. Femoral Bone Graft

Yes ☐ (1)

No ☐ (2)

If Yes

Autograft ☐ (1)

Allograft ☐ (2)

Not applicable ☐ (8)

PRE-OPERATIVE OUTCOME MEASURES

9. Oxford Hip Total Score ☐☐

10. Harris Hip Total Score ☐☐☐

11. EQ-5D Scores

Mobility ☐

Self Care ☐

Activity ☐

Pain ☐

Anxiety ☐

EQ-5D Descriptive score ☐☐☐

12. VAS score ☐☐

Case Report Form 1 completed by:

Name ……Signature ……..……..……

Date ……..